REMARKS/ARGUMENTS

Because the claims have not been amended, no new matter has been added.

Applicants thank Examiner Long for the courtesy of meeting with their undersigned representative on April 14, 2009. During this meeting, the obviousness rejection of Claims 12-19 as being unpatentable in over Upholt, Xie and Matsumoto was discussed.

Two main issues were discussed. First, that the Xie database entry is not believed to be applicable prior art against the claims of the present application. Second, the references do not provide the requisite reasonable predictability of success.

Xi et al describes a sequence and there are two dates reported on that database entry. The first date at the top of the entry (ID AAK98621) indicates a 8-Feb-2006 date. As the present U.S. application was filed from a PCT filed on November 14, 2003, this date of Xi et al is not available to cite against the claims of the present U.S. application. During the aforementioned meeting, the Examiner also noted that the Xie database entry also indicates that there was a "Direct Submission" and that it was "Submitted (19-Jul-2001)"--see fields "Title" and "Journal" in the database entry. As stated in the Declaration of Dr. Yongzhi attached, the cDNA sequence encoding Chicken Type II collagen was submitted to GenbAnk on February 8, 2006 but did not submit the same sequence to Genbank on July 19, 2001. The earliest date as shown in Genbank is not correct.

Also as stated on a second Declaration from Dr. Yongzhi, there was a submission on July 19, 2001 but that submission was withdrawn and was not the same sequence as is reported in the cited AAK98621 database entry cited in the rejection.

As the sequence which is relied upon in the rejection was submitted after the filing date of the present application (PCT filing date), the rejection is not applicable to the claims of the present application.

At least one this basis, Applicants request withdrawal of the rejection.

As to the second point, Applicants understand that obviousness is likely found where: a combination of familiar elements according to known methods yields predictable results, a person of ordinary skill can implement a predictable variation, and something can be obvious to try (*KSR v. Teleflex*, 127 S.Ct. 1727 (2007)). Applicants also understand the holding in *Ex parte Kubin*, 83 USPQ2d 1410 (BPAI 2007) recently affirmed by the Court of Appeals for the Federal Circuit (April 2009).

However, unlike these situations, the art cited in the rejection and in particular the cDNA that is the subject of the claims was not simply a matter of running through routine experiments yielding predictable results but rather that given the complexity of the cDNA that the Applicants have isolated, there were a number of not so routine experiments and that the result was not reasonable expected based on routine experiments. This is true regardless of the sequences (nucleotide and amino acid) cited from the Upholt and Xie GenBank database entries.

Upholt only describes a genomic sequence (and only a partial one as the N-terminus was not identified-see pp. 2327) and the difficulty in obtaining the cDNA sequence and the number of important and critical steps needed to obtain the cDNA clone. It should also be noted that Upholt's paper was almost 20 years before the inventors reported their clone in the PCT application and clearly that was evidence of the difficulty and long felt but unmet need of obtaining a cDNA encoding Chicken collagen type II.

Upholt describes a genome encoding chicken type II procollagen that consists of 46 exons and 45 introns (see, for example, Figure 2 and Table 1 of Upholt). Further, Upholt describes, at page 2327, "Although we have no data regarding the NH_2-terminal regions of the chicken $\alpha 2$(II) procollagen gene, available data for the chicken $\alpha 2$(I), the human α(I), the human $\alpha 1$(II), the rat $\alpha 1$(II) gene and chicken $\alpha 1$(III) genes suggest this region has diverged considerably" (underlining emphasis added). Accordingly, based upon the admissions of Upholt, Applicants submit that a person of ordinary skill in the art could not obtain the full-length genomic cDNA sequence from the disclosure of Upholt, and could not therefore clone the full-length sequence of the CCOL2A1 gene even with the sequence of Xie.

The cDNA has a complicated structure with a high GC content, frequently repeated sequences and many nonspecific binding sites to the primers making its cloning extremely difficult. It is rather difficult to amplify long DNA sequences with high GC content with PCR. That is because high GC content generates stable secondary structure hindering the DNA polymerase. Moreover, there may exist many nonspecific local renaturation sites to primers, which results in nonspecific amplification.

In contrast to the convention methods yielding reasonably predictable results, the Inventors solved the difficult problem of cloning this particular cDNA. The Inventors used analyzed the restriction site of the cDNA sequence in the CCOL2A13' domain and used restriction enzyme to incompletely digest the cDNA, then used PCR to the C-terminal domain. Directed to the high GC content in CCOL2A1, the Inventors used Taq enzyme which is can amplify GC-rich regions. Also, as CCOL2A1 is relatively long, the Inventors divided the CCOL2A1 cDNA into five fragments to subject each to PCR amplification, and make the amplified fragments with an overlap of at least 50 basepairs to allow the end-to-end connection using SOE-PCR. Finally, the Inventors obtained the full length CCOL2A1 cDNA of 4837bp, which included an open reading frame of 4260bp and a 3' nontranslated region of

520 bp. The deduced peptide of cco12a1, composed of 1420 amino acids, can be divided into signal peptide, N-propeptide, N-telopeptide, triple helix, C-telopeptide and C-propeptide.

The teachings of Matsumoto do not remedy the deficiencies of Upholt. Applicants note that Matsumoto does not appear to describe or suggest any experimental data about a chicken type II collagen made by recombinant genetic techniques, and therefore cannot remedy the deficiencies of Upholt, Xie and Matsumoto

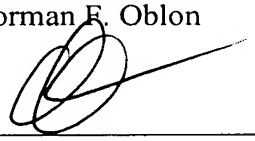
Thus, Matsumoto, Xie and Upholt do not describe or suggest the isolated polynucleotide sequences of present Claims 12 and 13, and the claims depending therefrom.

Withdrawal of the obviousness rejection is respectfully requested.

Applicants submit the present application is now in condition for allowance. Early notification to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Daniel J. Pereira
Attorney of Record
Registration No. 45,518

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)

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